Supplementary Table 1 CONSORT checklist

Section/Topic	Item no.	Checklist item	Reported on page no.
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3
	2b	Specific objectives or hypotheses	3
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	4 and ref. 10 (study primary manuscript)
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	4 and ref. 10 (study primary manuscript)
	4b	Settings and locations where the data were collected	4 and ref. 14 (study

			primary manuscript)
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	4 and ref. 10 (study primary manuscript)
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	4 and ref. 10 (study primary manuscript)
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	ref. 10 (study primary manuscript)
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	ref. 10 (study primary manuscript)
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	ref. 10 (study primary manuscript)
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	ref. 10 (study primary manuscript)

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	ref. 10 (study primary manuscript)
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	ref. 10 (study primary manuscript)
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	5
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	5
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	ref. 10 (study primary manuscript)
	13b	For each group, losses and exclusions after randomisation, together with reasons	ref. 10 (study primary manuscript)
Recruitment	14a	Dates defining the periods of recruitment and follow-up	4 and ref. 10 (study primary manuscript)
	14b	Why the trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1

Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	5-7, all figures and tables
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	5-7, all figures and tables
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	5-7, all figures and tables
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	5-7, all figures and tables
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	ref. 10 (study primary manuscript)
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	8
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	7-8
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	7-8
Other information			
Registration	23	Registration number and name of trial registry	2
Protocol	24	Where the full trial protocol can be accessed, if available	N/A

Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	10

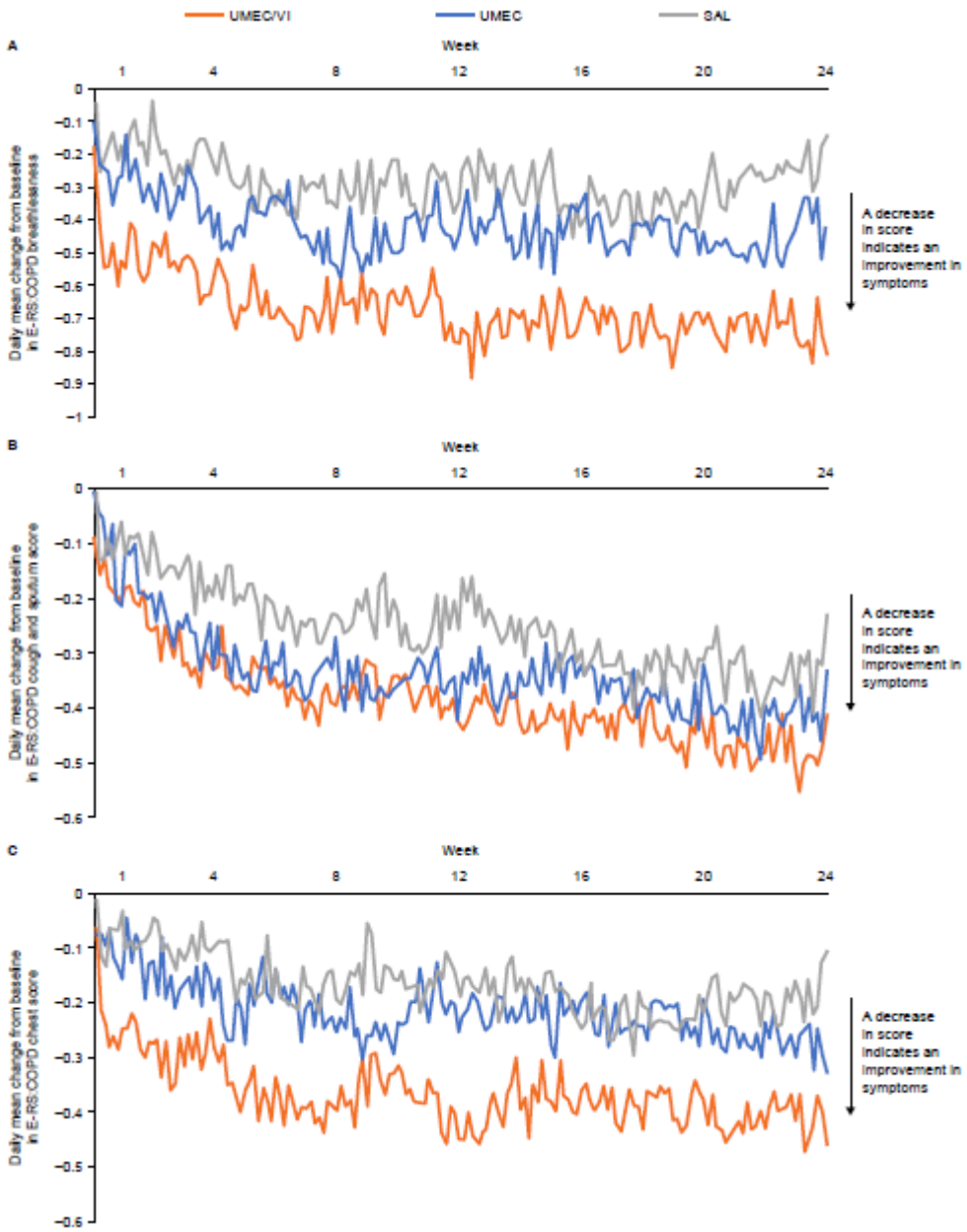
Supplementary Table 2 Patient demographics and baseline characteristics by E-RS:COPD responder status at Weeks 1–4

	E-RS:COPD responders at Weeks 1–4				E-RS:COPD non-responders at Weeks 1–4			
Characteristic	**UMEC/VI (n=236)**	**UMEC (n=202)**	**SAL (n=188)**	**Total (n=626)**	**UMEC/VI (n=567)**	**UMEC (n=594)**	**SAL (n=617)**	**Total (n=1778)**
Age, years, mean (SD)	64.6 (8.2)	64.2 (8.6)	64.2 (9.4)	64.4 (8.7)	64.7 (8.4)	65.1 (8.5)	64.4 (8.3)	64.7 (8.4)
Female, n (%)	105 (44)	91 (45)	86 (46)	282 (45)	208 (37)	233 (39)	254 (41)	695 (39)
Current smoker at screening, n (%)	124 (53)	108 (53)	103 (55)	335 (54)	264 (47)	283 (48)	308 (50)	855 (48)
Moderate COPD exacerbation in prior year[a], n (%)	32 (14)	31 (15)	30 (16)	93 (15)	91 (16)	91 (15)	115 (19)	297 (17)
Duration of COPD, years, mean (SD)	8.9 (7.2)	7.6 (5.6)	8.7 (6.2)	8.4 (6.4)	8.7 (6.8)	7.9 (6.1)	8.1 (6.9)	8.3 (6.6)
Maintenance-naïve, n (%)	75 (32)	83 (41)	81 (43)	239 (38)	172 (30)	165 (28)	167 (27)	504 (28)
Post-salbutamol % predicted FEV_1, mean (SD)	54.6 (13.2)	54.3 (11.7)	56.0 (13.2)	54.9 (12.7)	55.1 (12.6)	56.4 (12.9)	55.5 (12.7)	55.7 (12.7)
E-RS:COPD total score, mean (SD)	12.2 (5.0)	13.2 (5.7)	13.1 (5.4)	12.8 (5.4)	10.0 (5.7)	9.9 (5.7)	9.6 (5.6)	9.8 (5.6)
CAT score ≥20 at screening	105 (45)	111 (55)	109 (58)	325 (52)	226 (40)	243 (41)	224 (36)	693 (39)
Rescue salbutamol, puffs/day, mean (SD)	2.6 (2.8)	2.7 (2.7)	2.6 (2.4)	2.6 (2.7)	2.0 (2.4)	2.0 (2.2)	2.0 (2.5)	2.0 (2.4)
Percent rescue salbutamol-free days, mean (SD)[b]	33 (39)	33 (40)	31 (38)	33 (39)	42 (43)	42 (42)	42 (42)	42 (42)

[a]Number of exacerbations requiring oral or systemic corticosteroids and/or antibiotics (moderate) in 12 months prior to screening (patients with >1 moderate exacerbation or with a severe exacerbation [requiring hospitalisation] were excluded); [b]percentage of rescue-free days from Day -28 to Day -1 inclusive.

CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; E-RS:COPD, Evaluating Respiratory Symptoms in COPD; FEV_1, forced expiratory volume in 1 second; GOLD, SAL, salmeterol; SD, standard deviation; UMEC, umeclidinium; VI, vilanterol.

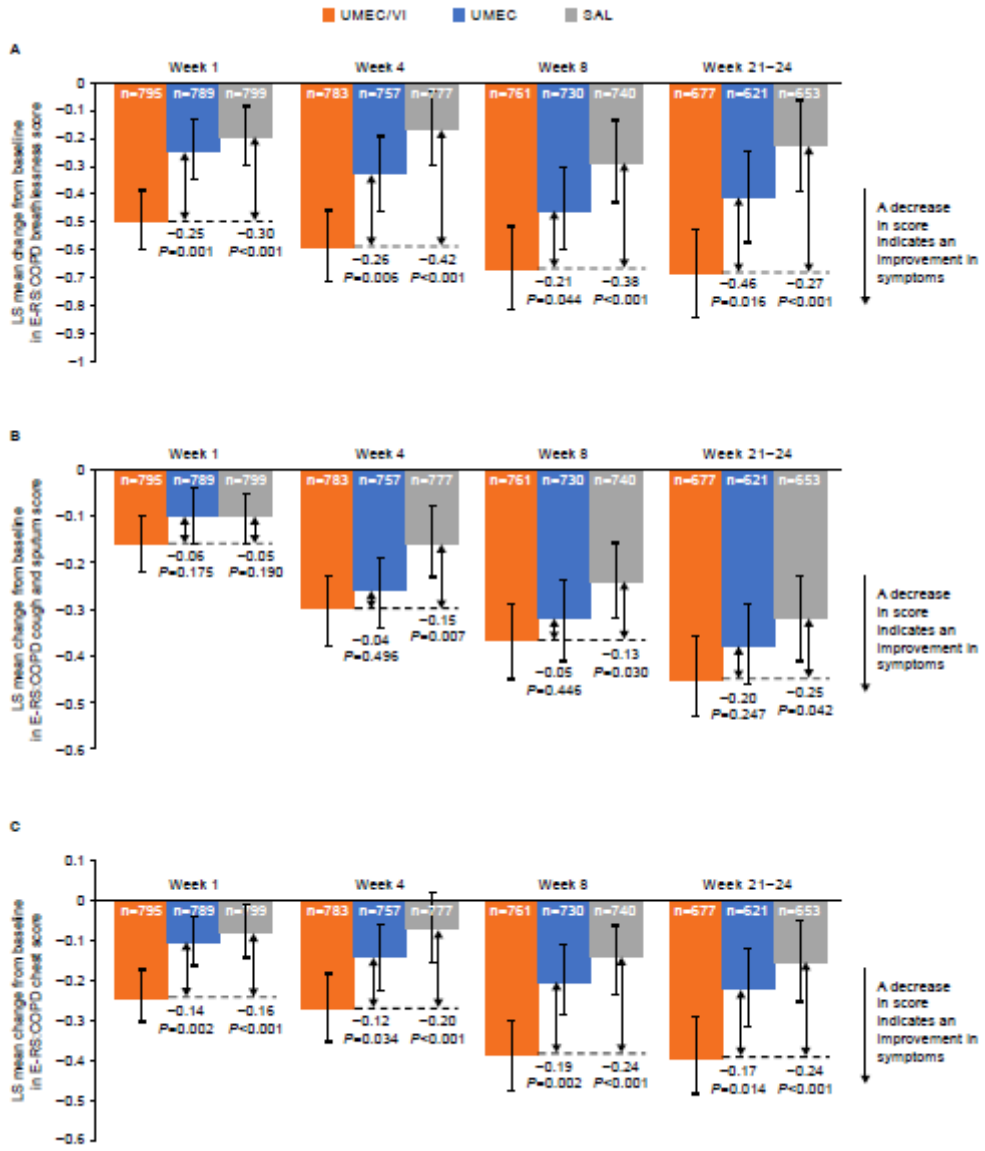
Supplementary Figure 1 Daily mean change from baseline[a] over time in E-RS:COPD breathlessness score **(A)**, cough and sputum score **(B)** and chest symptoms score **(C)**



[a]Baseline (Day 0) is defined as the average of the measurements recorded from Day -28 to -1 inclusive.

E-RS:COPD, Evaluating Respiratory Symptoms in COPD; SAL, salmeterol; UMEC, umeclidinium; VI, vilanterol.

Supplementary Figure 2. LS mean change from baseline in breathlessness score **(A)**, cough and sputum score **(B)** and chest symptoms score **(C)**



Analyses for Weeks 21–24 were pre-specified, and for Weeks 1, 4 and 8 were conducted post hoc.

E-RS:COPD, Evaluating Respiratory Symptoms in COPD; LS, least squares; SAL, salmeterol; UMEC, umeclidinium; VI, vilanterol.